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RADIATION INJURY AND AUTOLYSIS

-USSR-

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FOREWORD

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The reaction of cells of living organisms exposed to ionizing radiations displays a certain monotypic character in form of more or less marked paranecrotic changes (Nasonov, Aleksandrov, 1940). It is particularly important to note that these changes are brought about through the direct participation of proteolytic ferments (Geyl'brun, 1957). In this respect they very much resemble the effects observed in cell and tissue autolysis. Autolysis is generally understood to mean the posthumous disintegration of tissues due to their self-digestion.

Analogous effect is observed in the life of a multicellular organism in form of cell cytolysis and aseptic necrosis of tissue sections. In the latter case the disintegration of tissue proteins is brought about not only by the ferments of disintegrating cells but also by the ferments produced by the surrounding healthy tissues, as well as by white blood cells.

In principle the mechanism of their action differs in no way from the action of autolytic ferments (Mechnikov, 1901). The main accent in the latter work is on the analysis not of post-humous changes in cells and tissues but in those vital destructive effects which lead to some sort of functional disturbances in the living organism, or to the loss of active life. There are grounds to assume that these effects take their course in accordance with the autolytic mechanism. It is indeed difficult to expect that a process fully identical to the autolytic could evolve in life. It appears impossible, however, to reject the possibility of appearance of a slowly developing and less marked process resembling the autolytic, though it be on the basis of the similarity of changes recorded in radiation sickness and in autolysis.

It is a common knowledge, moreover, that the analogous effect is observed in a whole series of other pathological conditions: starvation, infectious diseases, aseptic resolution of tumors, and in many other cases associated with tissue necrosis and cell cytolysis in vivo (Ramond, 1908; Kochneva, 1917; Rosenberg, 1923; Berenbom, Chang, Stowell, 1954, 1955; Gallagher, Judah, Rees, 1954). The elements of the autolytic process occur also in the normal vital activity of the organism (Kizel', 1940). The ionizing radiations may in this case magnify their manifestation.

The concept of development of an autolysis-like process in an irradiated organism helps us to seek drugs which could be used in radiation sickness. For example, the American researchers Lushbaugh, Hughes, and Hale (1956), working from such premises,

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developed a preparation (anti-tryptic inhibitor) which, according to their data, produces a good effect when injected into animals during the ailing period. In this case the data pointing to an intensified radiation effect produced by the cysteine-type preparations when used within a certain period following the irradiation, become understandable (Khamayde and Mochalina, 1959; Benevolenskiy, 1959). Recognition of the stated surmise may help also to clear up many aspects of the mechanism of tissue disintegration as a result of radiation sickness. It is obvious indeed that the task becomes very simple when the opportunity is at hand to use results readily obtainable in tests in vitro.

This survey concerns the review of literature pertaining to the problem at hand, together with an attempt to explain these data in the light of modern ideas regarding the biological effects of ionizing radiations.

Autolysis of Tissues Irradiated In Vitro and In Vivo

The first examinations of tissues irradiated in vitro showed that their autolysis is somewhat faster in comparison with the normal tissues. These examinations were usually conducted with the aid of biochemical methods (most frequently, the rate of accumulation of free nitrogen) or by the study of morphological changes in cells and tissues. The acceleration of autolysis has been revealed particularly clearly in irradiation of tumor tissues and the spleen, i.e. in objects most sensitive to radiation. Such mechanism has been recorded less clearly for the liver tissue (Neuberg, 1904; Löventhal, Edelstein, 1908; Minami, 1912; Hajos,

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Hafhauser, 1924; Mayer, Bering, 1911; Herzger, 1927; Gasul' and Polyakova, 1929). In a number of cases no accelerated autolysis of irradiated tissues was recorded (Bickel, Minami, 1911; Herzger, 1927; Varshavskaya, Ledanov and Sterkin, 1935).

More representative results have been obtained in the study of tissue autolysis in irradiated animals. Virtually as a rule, they were autolyzed much faster than the tissues of normal animals (Heile, 1904; Warren, Whipple, 1922; Herzger, 1927; Berneim and others, 1956; Libinzon, 1957; Grayevskaya and Keylina, 1959; Grayevskaya, 1957; Manoylov, 1957; Tokarskaya, 1958a, 1958b, 1959). Analogous data have been recorded on fish (Epshteyn and Lavrovskaya, 1959) and plants (Milova, 1936; Sosedov, Vokar, Pod"yapol'skaya and Tertsovskiy, 1957).

The earliest and most marked variations in the rate of autolysis occurred in bone marrow, intestines, spleen, liver, and muscles. For kidney and brain tissues the rate of autolysis was slightly higher than normal or was not recorded at all. Aside from the type of tissue, the intensity of autolysis of the organs of irradiated animals depended on the dose of ionizing radiation and the duration of radiation sickness. The rate of autolysis of irradiated tissues clearly surpassed that of un-irradiated tissues when lethal or sublethal doses were used. In smaller doses the autolysis of irradiated cells and tissues proceeds at times with a lesser intensity than the autolysis of un-irradiated cells and tissues (Manoylov, Grayevskaya and Shimanovskiy, 1955). Tissues obtained at the peak of radiation sickness undergo the most rapid autolysis. Autolysis of irradiated tissues occurs

less intensively at the beginning and concluding stages of radiation sickness (Warren, Whipple, 1922; Tokarskaya, 1959).

The autolytic process in irradiated tissues has apparently also certain qualitative differences compared to the autolysis in un-irradiated tissues. For example, according to the data obtained by R.Ye. Libinzon (1957) and Z.V. Tokarskaya (1959) the process is not intensified by the usual autolysis activators in normal tissues—acetylcholine and hydrogen sulfide.

The more intensive autolysis of irradiated tissues is shown also by the data on their increased hemolytic activity, or, otherwise, the formation of tissue hemolysins called collectively the hemolytic factor (Mochalina, 1957; Kudryashov, 1956, 1957; Benevolenskiy, 1957a, 1957b; Benevolenskiy and Blokhina, 1959; Khamayde, 1957; Korol' and Mednik, 1958).

The development of the hemolytic factor requires a lengthy incubation of aqueous-salt tissue extracts with erythrocytes at 37°, during which the autolytic process inevitably takes place. It is a general knowledge, moreover, that autolysis of any tissue always produces tissue hemolysins in it (Gorkin, 1953; Ponder, 1955).

Thus, a specific portion of the hemolytic factor is formed in the tissues of irradiated animals as a result of their accelerated autolysis in vitro. It will be shown below that the formation of the hemolytic factor is not due to the posthumous autolysis alone.

The formation of the hemolytic factor has been recorded in the most diverse tissues of irradiated animals (Mochalina,

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1957; Kudryashov, 1957) and in all component parts of cellular protoplasm: mitochondria, microsomes, and hyaloplasm (Benevolenskiy and Blokhina, 1959). It has not been found in the liver nuclei of irradiated rabbits (Korol' and Mednik, 1958). The quantity of the hemolytic factor determinable in tissues corresponds approximately to the earlier established distribution of autolytic intensity in the organs of irradiated animals. It is interesting to note, for example, that the largest quantity of this factor is found in the intestines, spleen, liver, and, to a vastly smaller degree, in kidneys and brain (Mochalina, 1957).

Comparative Characteristics of Changes Observed in Radiation Sickness and Autolysis

As a consequence of exposure to radiation the organism undergoes a variety of changes, beginning with the hardly noticeable physicochemical disturbances and ending with the cytolysis of cells and necrosis of tissues. These changes occur characteristically on the background of an altered metabolism and suppressed mitotic activity of cells in the irradiated organism (Ivanov, Balabukha, Romantsev and Fedorova, 1956; Grayevskiy and Shapiro, 1959). In this connection the irradiated organism develops conditions for the progress of destructive changes analogous in many respects to the conditions taking place in posthumous autolysis of tissues. It may be expected, therefore, that the tissue disturbances occurring in radiation injury and in autolysis are in many ways analogous.

No specially conceived investigations have been conducted

in the above indicated direction. This being so, it is impossible to supply a detailed comparative description of changes occurring in radiation sickness and autolysis. Noteworthy in this framework is the fact that the one and the other changes occur in any cell and tissue of living organisms. It is interesting to note the correlation in the distribution of susceptibility of various cells to disintegration induced by radiation exposure and autolysis. For example, on the basis of morphological disturbances the cells are arranged in the following order of their susceptibility to radiation: blood forming cells, functional cells of endocrine glands, sex cells, epithelial cells of gastro-intestinal tract; cells of liver, lungs, kidneys; cells of connective tissues, muscular cells, and nerve cells (Ellinger, 1951). Cells of tumor tissues are also very susceptible to radiation. Similar order prevails also in the distribution of the posthumous autolytic intensity of the ennumerated cells (Khalatov, 1944).

Thus the cells that are autolyzed faster, change faster and more profoundly when exposed to radiation. This feature had been noted by the original radiobiologists, and constituted one of the reasons for the application of ionizing radiations in treatment of cancer diseases (Neuberg, 1904).

One of the indices of radiation injury is the fatty degeneration of tissues. It is observed in the most diverse biological objects that have been exposed to ionizing radiations: unicellular organisms, plants, and animals (Nadson, 1920; Nadson and Rokhlina, 1934; Nikitin, 1938, 1957; Ellinger, 1945). The fatty degeneration process, or the lipophanerosis effect, as it

was called in the beginning, always occurs in the posthumous autolysis of tissues. It is associated with the dissociation of tissue lipoproteins and may be of reversible or irreversible character, depending on circumstances (Kizel', 1940).

The morphological changes observed in radiation sickness and in autolysis have therefore a number of features in common.

Numerous biochemical data attest to the fact that a progressive disintegration of various cellular protoplasm components occurs in radiation sickness; that this disintegration is particularly intense at the peak of the sickness and in the preagonal period. It displays itself in a drop in tissue proteins and in an increase in residual nitrogen in form of urea nitrate, creatinine, ammonia, etc. Sometimes the urine from an irradiated organism reveals also undecomposed proteins (Ord, Stocken, 1953; Pigalev, 1954; Kuzin and Strazhevskaya, 1957; Ivanov, Balabukha, Romantsev and Fedorova, 1956). All these disturbances are undoubtedly due, as in autolysis also, to the action of proteolytic ferments or, put another way, they are accomplished in accordance with the mechanism of posthumous autolytic process.

An additional proof of this circumstance are the data showing the increased activity of autolytic ferments during radiation sickness; this applies specifically to protease, phosphatase, lipase, and nucleodepolymerase (Reprev, 1926; Cherkes and Natanson, 1936; Feinstein, Bollin, 1953; Du Bois, Petersen, 1954; Bacq, Alexander, 1955; Feinstein, 1956; Grayevskaya, 1957; Ginzburg, Pandre and Binus, 1957; Weymonth, 1958; Tokarskaya, 1959; Prokudina, 1959; Libinzon, 1959).

These changes do not occur immediately after the exposure to radiation in doses of the minimally lethal order. The activity of the above noted ferments increases only after a few hours or days and grows gradually, diminishing at the concluding stages of the fatal radiation sickness. The speed of appearance of observable changes and their direction depend in a large measure on the type of tissue involved.

It is important to note that analogous dynamics of changed activity of such ferments is recorded in posthumous autolysis (Berenbom, Chang, Betz, Stowell, 1955, 1958; Van Lanker, Holtzer, 1959).

Interesting data have been obtained in investigations of the overall activity of the ferments causing the formation of the hemolytic factor (tissue hemolysins) during radiation sickness and autolysis (Benevolenskiy, 1957a, 1957b). These ferments comprise mainly lipases and proteases (Ponder, 1951; Gorkin, 1959).

The complex of above noted ferments existing in the liver of rats exposed to roentgen rays amounting to 1,000 roentgens increases its activity markedly even within an hour following the exposure. The increased activity is recorded for two-three days, being replaced by a diminished activity toward the death of animals.

In posthumous autolysis of the liver of normal animals the total activity of ferments participating in the formation of tissue hemolysins also increases during the first hour of autolysis, diminishing rather rapidly thereafter and reaching low values after four hours of autolysis.

The results of these tests fully corroborate the data derived from the study of the activity of individual ferments comprising this complex. Moreover, they show that a portion of the hemolytic factor of tissues of irradiated animals is actually formed as a result of vital processes. The latter is confirmed also by examinations of the hemolytic properties of boiled tissue extracts from irradiated and normal animals. It has been established that the hemolytic activity of these extracts, prepared from the liver of irradiated animals, is always higher than the activity of extracts prepared from the liver of normal animals. An intensified autolysis of liver extracts from irradiated animals during the incubation with erythrocytes cannot be observed in this case. Hence the excess of the hemolytic factor in the extracts from irradiated animals, in comparison with the extracts from un-irradiated animals, can be explained only by its partial formation in the course of vital processes.

Yu.B. Kudryashov (1957) and V.N. Benevolenskiy (1957) have shown that the hemolytic factor of tissues of irradiated animals differs in no respects from the hemolysins formed in autolysis of normal tissues. According to modern data, these hemolysins are comprised of substances mainly of lipoid nature: unsaturated fatty acids, lysolecithins, and steroid compounds. In normal state they are always associated with proteins and a number of other compounds, and do not as a consequence exhibit their hemolytic activity. When these complexes are dissociated the lipid hemolysins are set free, imparting thereby the hemolytic properties to the tissues. As has been noted earlier, this dissociation is caused by the complex of

ferments taking part in the posthumous autolysis of tissues (Gorkin, 1953; Ponder, 1955; Kazayev, 1957).

A number of analogous physicochemical changes in tissues have been recorded in radiation sickness and in autolysis. For example, the ohmic and capacitive resistance of the liver tissue, measurable at various frequencies, changes in one and the same direction. The same phenomenon occurs in the kinetics of accumulation of filamentous formations observed in the electron microscopy of aqueous extracts of mouse and rat liver (Polivoda, 1957; Polivoda and Zolotova, 1958; Benevolenskiy, 1957).

The data in literature show, then, that the autolysis of tissues irradiated in vivo and in vitro accelerates markedly. In addition, there is noted a certain analogy in the changes observable in tissues during the development of radiation sickness and autolysis. Hence it may be concluded that the disintegration of tissues occurring in radiation sickness proceeds in apparent conformity with the mechanism of autolysis.

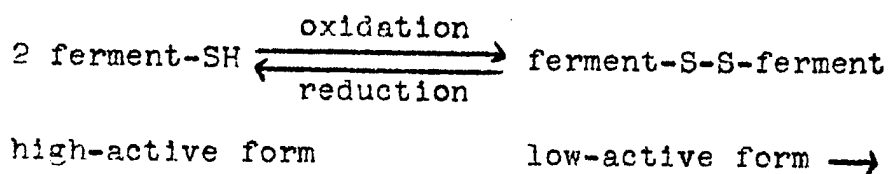### Mechanism of Emergence and Development of the Autolytically Congruent Process in Radiation Sickness

In order to answer the question why and how the emergence and development of an autolytically congruent process takes place in radiation sickness, it is necessary to examine briefly the modern views of the mechanism of posthumous autolytic process. Posthumous autolysis occurs in each tissue due to the action of autolytic ferments, with the greatest weight in this case being

attributed to proteolytic ferments (Gol'dshteyn, 1938; Bradley, 1938; Kizel', 1940). In this connection the very term "autolysis" is frequently substituted by the term "proteolysis". Such substitution is in no way justified: autolysis is a much more encompassing concept; it includes not only the concept of disintegration of proteins but also of many other compounds, for example, lipids, carbohydrates, nucleic acids, as well as their mutual combinations and their combination with proteins. Nevertheless the ideas about the mechanism of development of posthumous autolytic process have been formed principally on the basis of results obtained from examinations of proteolytic ferments containing the SH-group.

According to these ideas such ferments exist in the normally functioning tissue in a low-active form in which their sulfhydryl groups are combined by the disulfide bond. In general form these ferments are designated by the formula ferment-S-S-ferment. The low-active form of proteolytic ferments is easily converted into the high-active form by the action of various reducible substances, for example, cysteine or reduced glutathione. In this form they have the formula of the type ferment-SH. With the aid of oxygen and other oxidizing agents the high-active form of ferments can be reversed into the low-active form. Thus the general equation of this reversible reaction has the following form

$$2 \text{ ferment-SH} \underset{\text{reduction}}{\overset{\text{oxidation}}{\rightleftharpoons}} \text{ferment-S-S-ferment}$$

high-active form   low-active form →

It follows from this equation that posthumous autolysis emerges as a result of suppression of oxidation-reduction processes, which sets in due to the lack of oxygen and nutrient substances.

Such schematic framework lies at the foundation of the majority of early hypotheses regarding the mechanism of development of the autolytic process in vitro, and the emergence of similar reactions in vivo (Hellerman, Perkins, 1934; Bradley, 1938; Gol'dshteyn, 1938; Blagoveshchenskiy, 1940).

In more recent times the English researchers Gallagher, Judar and Rees (1956) have studied in detail the entire succession of biochemical changes taking place in autolysis of the liver tissues in normal animals. They have found that the earliest changes in posthumous autolysis occur in the system of oxidizing phosphorylation, followed by the disruption of glycolysis and tissue respiration, and ending finally with proteolysis of tissue proteins accomplished by activated proteases. Analogous data have been derived also by other researchers (Berenbom, Chang, Stowell, 1954; Van Lanker, Holtzer, 1959).

At the foundation of the cited hypotheses lie the purely chemical assumptions which do not take into account the fact that autolysis ordinarily takes place not in a homogeneous medium but in a system having a definite structure. It is particularly imperative that the latter circumstance be taken into account when the possibility of development of such process is discussed.

It is a known fact that the disruption of internal physico-chemical structure of tissues may of itself lead to the development

of the autolytic process as a result of liberation of hydrolytic ferments from their combined state (Oparin, 1936; Kursanov, 1940; Sisakyan, 1954; Meysel', 1950).

The structures of living tissues are, as is known, unstable. Their preservation is accomplished at the expense of the energy supplied by the processes of tissue respiration through the oxidizing phosphorylation system. There is in turn a close reverse relationship (Neyland and Shtumpf, 1958). Hence it follows that the apparent cause of development of the autolytically congruent process in an irradiated organism may be, first, the primary disruption of the physicochemical structure of tissues and, second, the suppression of the processes generating and transmitting the energy for maintenance of this structure.

The first attempt at explanation of the causes of development of the autolytic process in an irradiated organism belongs to Neuberg (1904). According to his hypothesis, at the base of this phenomenon lies the dissimilar radiation susceptibility of the oxidizing-reducing and autolytic ferments. The former are, as he had supposed, more susceptible to radiation than the latter. This means that the radiation exposure must be followed by the emergence of a disproportion in the activity of these two fermentative groups, which precisely leads to the development of the autolytic process.

Numerous researches of recent years show, however, that a suppression of oxidizing-reducing processes and, consequently, also of ferments associated with these processes, does not take

place immediately following the irradiation. On the contrary, especially in exposure to small doses of ionizing radiations, this period is frequently characterized by the activation of vital processes, including an intensification of synthesis and tissue respiration processes. The suppression of the oxidizing-reducing process occurs usually at later stages of radiation sickness (Du Bois, Petersen, 1954; Bacq, Alexander, 1955; Ivanov, Balabukha, Romantsev, Fedorova, 1956; Kuzin, 1956; Tarusov, 1958; Piri, 1958; Golubentsov and Sazykin, 1960). The development of autolysis-like process in an irradiated organism is thus evidently not associated with the suppression of oxidizing-reducing ferments.

It may be thought that this process emerges as a result of disruptions in the oxidizing phosphorylation system. As has been noted earlier, the analogous causal relation for the posthumous autolytic process has been established. In fact, as Meysel' (1955) and Van-Bekkum (1958) have shown, the oxidizing phosphorylation system is the first to be affected in irradiated organism. This coincides also with certain morphological data pointing to the major radiation susceptibility of mitochondria in which the oxidizing phosphorylation mainly takes place (Nadson and Rokhlina, 1934). It must be noted beforehand, however, that this process takes place to a lesser degree also in other parts of cell protoplasm and, according to some data, even in the nucleus (Neyland and Shtumpf, 1958). Therefore the assumption that the autolysis-like process emerges in an irradiated organism as a result of suppression of the oxidizing phosphorylation is corroborated by data available in modern literature. But the

question arises: what causes the suppression of oxidizing phosphorylation? There are no clear data pointing to the direct affection by ionizing radiations of fermentative systems, as well as many other systems, associated with the oxidizing phosphorylation. In this case we may again refer to the results of analysis of many literary data, which has been done in the concluding summary regarding the biochemical action of ionizing radiations (Du Bois, Petersen, 1954; Bacq, Alexander, 1955; Kuzin, 1956; Ivanov, Balabukha, Romantsev, Fedorova, 1956; Piri, 1958). Moreover, the earlier suppression of oxidizing phosphorylation is observed only in tissues susceptible to radiation.

The suppression of conjugate phosphorylation does not occur in "radioresistant" tissues of a muscle (Ivanov, Gaytskhaki and Korkhov, 1959). Thus the affection of the oxidizing phosphorylation in irradiated organisms cannot apparently be linked to the direct affection of the ferments. Up to now, however, this problem has not been resolved, so that some researchers maintain the opposite views (Manoylov, 1957; Van-Bekkum, 1958).

It is more probable that the cause of suppression of the oxidizing phosphorylation in an irradiated organism is the affection of normal physicochemical constitution of those structures in which it is accomplished. Taking into account their mass, a significant disruption of them cannot occur as a result of direct action of ionizing radiations, especially in doses less than the minimum lethal. In this connection an allowance

must be made for the presence of some sort of intensifying mechanisms of the primary radiation effect.

A number of researchers believe today that the intensification of the primary radiation effect is conditioned by physicochemical reactions resembling those occurring in proteins, fats, and nucleic acids in irradiation in vitro (Tarusov, 1954, 1958; Benevolenskiy, Korogodin, Polikarpov, 1957; Kuzin, 1958). Virtually as a rule these reactions take place only in the presence of oxygen, i.e. they are oxidizing. It is exceedingly important to note that similar reactions may lead to the disruption of normal physicochemical structure of the basic macromolecular components of the nucleus and cytoplasm: the nucleo- and lipoproteins.

It has been established in particular that in oxidation of the lipid constituent of lipoproteins the latter break up into their component parts. This has been observed in exposure of lipoproteins to ultraviolet rays (Deborin, 1956) and also when they are kept in air (Cohn, 1949; Roy, Devissen, Crepsi, 1954; Oncley, Frank, 1953). Indications to such possibility can be found in Lepeshkin's prolific works. According to his data the disintegration of tissue lipoproteins induced by various external influences is closely associated with the structure of their lipid constituent. The lipoproteins containing fats with double and triple bonds, i.e. the most easily oxidized lipoproteins, possess a marked capacity for dissociation; this feature has furnished the basis to compare them even to explosive substances (cited from Kizel', 1940).

It is extremely difficult to find real proofs of the

origin and development of the chain oxidizing reactions caused by ionizing radiations in vivo. Resort must be made in this case to indirect proofs. In the first instance these include the attempts to detect intermediate products of chain reactions; these products are, as is known (Semenov, 1936), peroxides. Intensive research in this direction has resulted in the detection of analogous products (chiefly lipid peroxides) in the tissues of irradiated organisms (Horgan, Phylpot, 1954; Dubouloz, Dumas, 1955; Gintsburg, Pandre and Rinus, 1957; Belokonskiy and Rusev, 1959; Zhuravlev and Ganassi, 1959).

The majority of investigators have found lipid peroxides only during the initial stages of radiation sickness. However, A.I. Zhuravlev and Ye.E. Ganassi have recorded their accumulation in the rat liver for several days following the exposure to ionizing radiations in lethal dose. The latter circumstance points to the possibility of a prolonged course of primary oxidizing reactions in an irradiated organism. The definitive proof of this supposition requires the exclusion of influences of the lipoxidase ferment, since in a number of cases, for example, in exposure of plant objects to ionizing radiations, the activity of this ferment is intensified (Budnitskaya and Borisova, 1959).

Decomposition of protein complexes in association with other substances can occur in an irradiated organism as a result of denaturation reactions in the protein component. The latter is well known from the practice of treating the tissues with alcohol to obtain an increased yield of extractable lipids. Similar vital denaturation changes have been observed in tissues of

irradiated organisms (Aleksandrov and Dikovenko, 1955; Mishchenko and Fomenko, 1934; Kiselev, Buzini and Semina, 1955). It must be noted, however, that the vital denaturation changes are recorded only after several days from the time of radiation exposure. Despite repeated attempts, neither physicochemical nor immunological methods have succeeded in detecting these changes immediately following the exposure (Tarusov, 1954). Hence the primary reactions in proteins have evidently a lesser significance than the reactions in fats for disturbances in the physicochemical structure of the tissue.

Without going into a detailed discussion of this complex problem, which has been analyzed in some detail in B.N. Tarusov's papers (1954, 1958, 1959), we should like to call attention to a fundamental and apparently indisputable condition. It consists in the fact that any physicochemical reactions to the aftereffects developing in the irradiated organism may lead to a marked disruption of the normal tissue structure. As a consequence of the disruption of tissue structure there occurs a liberation of hydrolytic ferments which create conditions for the development of the autolytically congruent process. As a consequence, there apparently appears a disruption in the system of oxidizing phosphorylation of tissue respiration and synthesis. This in turn must lead to further intensification of decomposition processes analogous to the autolytic. It is precisely such sequence of events that seems to us more probable in explaining the mechanism of development of the autolysis-like process following the exposure of living objects to ionizing radiations.

It is possible also that disruptions in the tissue structure resulting from the primary physicochemical reactions lead in the first instance to the disruption of the synthesis and tissue respiration processes, leading in turn to the development of the autolytically congruent process of tissue disintegration. This conclusion is, however, in conflict with numerous data pointing to the fact that small doses of ionizing radiations stimulate the vital process, including respiration, synthesis, and reproduction (Ord, Stocken, 1953; Du Bois, Petersen, 1954; Bacq, Alexander, 1955; Sokurova, 1956; Timofeyev-Resovskiy, Poryadkova, Makarov and Preobrazhenskaya, 1957).

Along with the stated explanation of the original mechanisms of development of the autolysis-like process in an irradiated organism, the highly organized animals abound in secondary causes of intensification of this process. Foremost of these are the multiple disturbances in blood circulation and in the regulatory activity of the endocrine apparatus and the nervous system. Relatively few works in this direction have been carried out in recent period by Z.B. Tokarskaya (1958) and B.M. Grayevskaya and R.Ya. Keylina (1959).

The reversibility feature of the autolysis-like process is an extremely complex problem. A detailed discussion of it is outside the scope of this survey. Certain of the data pertaining to this problem have been examined in a recently published survey article authored by E.Ya. Grayevskiy and I.M. Shapiro (1959).

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